BIOCARE MEDICAL

GATA3, p63 and S100P:

An IHC Comparison Analysis in Bladder Cancer

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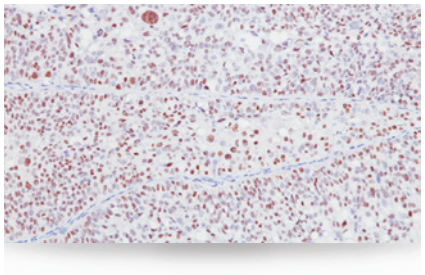

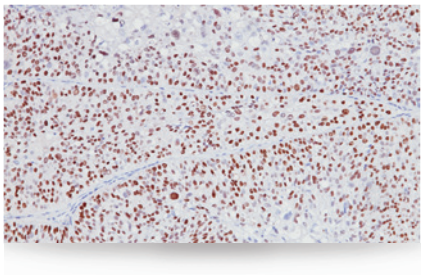

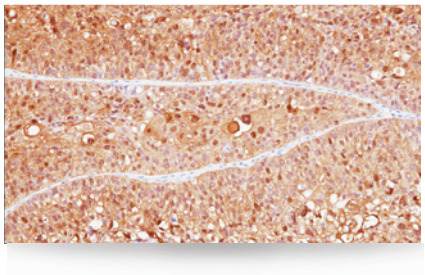

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Background

Bladder cancer frequently originates in the bladder lining (transitional epithelial cells), which consists of a mucosal layer of surface cells. More than 90% of bladder cancers originate in the urothelial lining. Establishing urothelial origin of the tumor is critically important; especially when prostate cancer is also being considered in differential diagnosis. Several studies have show p63 to be a sensitive marker for bladder cancers and negative in prostate and kidney cancers; however, only limited studies on GATA3 and S100P have been reported in bladder, prostate and kidney cancers. The aim of this study is to examine immunohistochemical staining characteristics of GATA3, p63 and S100P antibodies mainly on bladder transitional cell carcinomas (TCC), and compare staining expression of GATA3 and S100P on prostate and kidney cancers.

Design

Formalin-fixed paraffin-embedded TMA tissues of bladder cancers were constructed in-house or purchased commercially and processed in the usual manner for IHC analysis. All sections were retrieved in a modified citrate buffer in a pressure cooker at 125°C. Mouse monoclonal antibodies GATA3 and p63 and rabbit polyclonal antibody S100P were individually optimized and incubated for 30 minutes. Detection was using a micro-polymer HRP and visualization was with DAB.

Results

The sensitivity of GATA3, p63 and S100P in TCC are summarized in Table 1. GATA3 and p63 exhibit nuclear staining and S100P exhibits nuclear and cytoplasmic staining (Fig.1).

Discussion

GATA3 is relatively new marker in the clinical area and is an important regulator of T-cell development. It has been shown to be expressed in luminal A type breast cancer, intertwined in pathways with ERα. In this study, we compared sensitivity and specificity of GATA3, p63 and placental S100 (S100P). In the vast majority of cases of TCC, there was a co-expression of all three markers (Fig. 1) (Table 1).

Past studies have shown that GATA3 has been highly specific for breast and bladder cancers; and p63 has been shown to be negative for both prostate and renal cell carcinomas. In our study, GATA3 was also negative in prostate cancer (n=69) and renal cell cancers (n=69); except in renal urothelial carcinomas. The upper urinary tract TCC is estimated to occur in 5% of urothelial cancers.

Studies have shown S100P to be a sensitive marker for bladder cancers and negative in renal cell carcinomas, and mostly negative in prostate cancers. Our study confirmed this data.

There were several cases where either p63 or GATA3 were expressed individually (Fig. 2). In a separate category, one case of bladder adenocarcinoma was GATA3 and p63 was negative and S100P was strongly possible (Fig. 3). A possible pitfall was the expression of GATA3 in infiltrating inflammatory and T-cells (Fig. 4). T-cell staining of GATA-3 was confirmed by staining tonsil.

Conclusion

GATA3, p63 and S100P are highly sensitive and specific biomarkers for the differential diagnosis of urothelial carcinoma. This three biomarker panel may be employed to establish urothelial origin and may aid in cases of tumor of unknown origin.

Table 1: Transitional Cell Carcinoma: All Grades

Antibody	Cases	Positive	(+) %	Negative	(-) %
GATA 3	59	54	92%	5	8%
p63	59	53	90%	6	10%
S100P	59	55	93%	4	7%

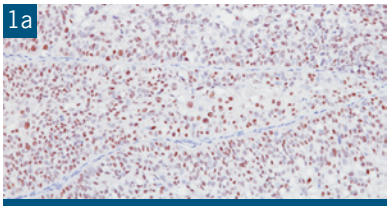
In Grade 3 (poorly differentiated) TCC, GATA 3 was the most sensitive marker (n=11) (Table 2).

Table 2: Transitional Cell Carcinoma: Staining according to Histologic Grade

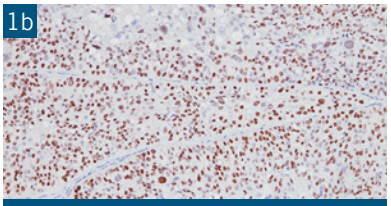
Grade 1-3	Grade 1 (11 cases)	Grade 2 (37 cases)	Grade 3 (11 cases)
GATA-3	10 (90.9%)	33 (89.2%)	10 (90.1%)
p63	11(100%)	32 (86.5%)	9 (81.2%)
S100P	11(100%)	33 (89.2%)	9 (81.2%)

GATA3 was 100% negative in prostate (n=68) and renal cell carcinoma (n=69). S100P was 100% negative in renal cell carcinoma and 98.6% negative in prostate cancer.

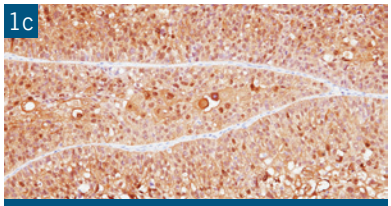
Figure 1



1a GATA3 nuclear staining in TTC

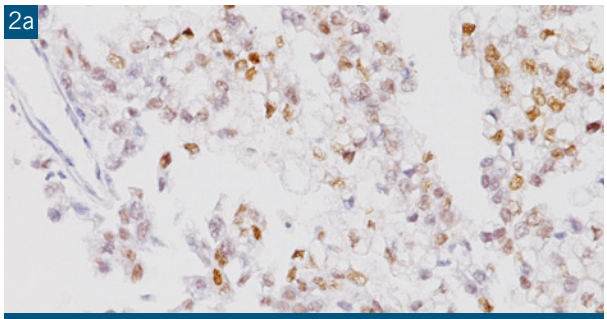


1b p63 nuclear staining in TCC

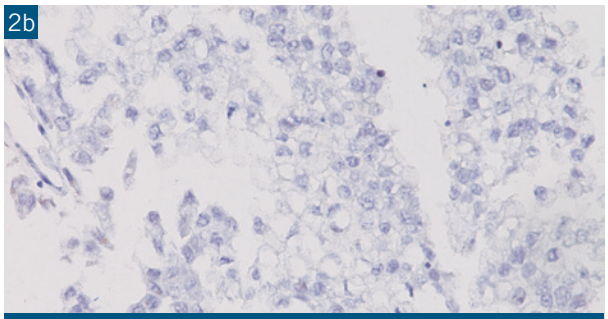


1c S100P nuclear & cytoplasmic staining in TCC

Figure 2

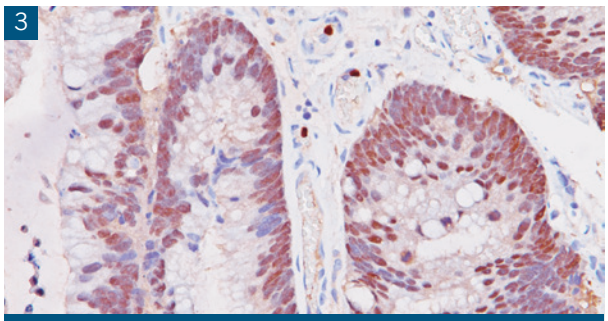


2a GATA3 was positive in a poorly differentiated TCC



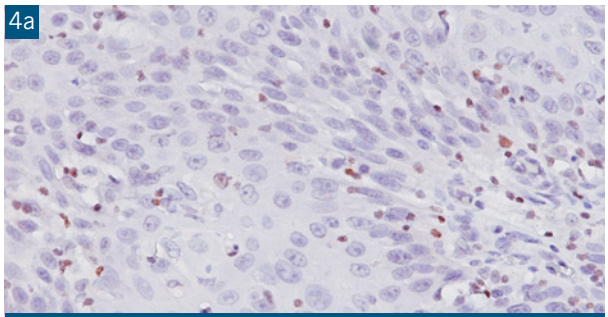
2b p63 was negative in a poorly differentiated TCC

Figure 3

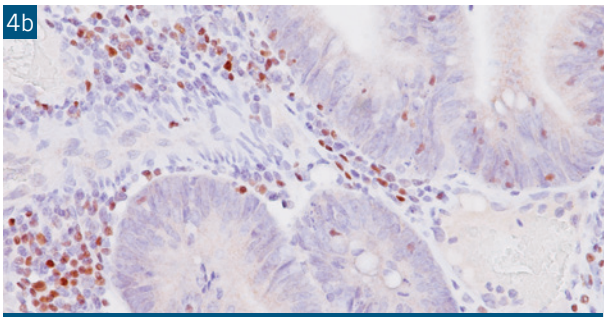


3 S100P was positive in a bladder adenocarcinoma (GATA3 & p63 were negative)

Figure 4



4a GATA3 stained inflammatory cells in bladder cancer



4b GATA3 stained infiltrating T-cells in bladder cancer

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